

## **Remarks**

### ***I. Status of Claims***

Claims 10, 11, 15-17, 22-49, 51-52, 57, 61, 66, 70, 72, 74, 76, 78, 83-84, 92, and 102 have been cancelled without prejudice or disclaimer. Claims 1 and 71 have been amended. Claims 103 and 104 are newly added. Upon entry of the current amendment claims 1-9, 12-14, 18-21, 50, 53-56, 58-60, 62-65, 67-69, 71, 73, 75, 77, 79-82, 85-91, 93-101 and 103-104 are pending in the application.

### ***II. Claim Amendments***

Claims 85 and 86 are amended herein to further clarify the invention recited in those claims.

### ***III. Claim Rejections- 35 U.S.C. §112***

The Office Action, mailed July 27, 2007, rejected claims 85 and 86 under 35 CFR 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention. The Office Action asserts that these claims require the cathode and anode, respectively, to be in the third region, although claim 1 requires these electrodes to be in either the first or second region. (Office Action, page 3).

The Applicants have amended claim 85 to recite that the cathode is in the first region, and have amended claim 86 to recite that the anode is in the first region. Accordingly, the Applicants respectfully request that the rejection of claims 85 and 86 under 35 CFR 112, second paragraph, be withdrawn.

### ***IV. Double Patenting***

The Office Action, mailed July 27, 2007, advised the Applicants that should claim 99 be found allowable, then claim 102 would be objected to under 37CFR 1.75 as being a substantial duplicate thereof. (Office Action, page 3).

The Applicants have cancelled claim 102, and therefore Applicants respectfully request withdrawal of the rejection.

**V. Claim Rejection - 35 U.S.C. §103**

***Tocci (U.S. Patent No. 3,715,295) in view of Elson (U.S. Patent No. 3,888,759)***

The Office Action, mailed July 27, 2007, rejected claims 1-4, 62, 71, 85-87, 91 and 94-102 under 35 U.S.C. §103(a) as allegedly being unpatentable over Tocci in view of Elson *et al.* Regarding obviousness, the U.S. Supreme Court recently clarified the legal standard: “Under § 103, scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented.” KSR Intern. Co. v. Teleflex Inc., U.S. 2007 (2007 WL 1237837 (U.S.)), at 6, citing Graham v. John Deere Co. of Kansas City, 86 S.Ct. 684. Furthermore, the Supreme Court clarified that a teaching away may be an indication of non-obviousness. K.S.R v. Teleflex at 18 citing United States v. Adams, 383 U.S. 39, 40 (1966)). Finally, the Supreme Court clarified that unexpected results support a conclusion of non-obviousness. *Id.*

Regarding a motivation to combine prior art references, the Supreme Court noted that it can be important to identify a reason to combine elements from different references. *Id.* at 13. The Supreme Court warned that “A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning.” *Id.* at 16, citing Graham, 393 U.S., at 36. “A patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. See KSR Int’l v. Teleflex Inc., U.S. Supreme Court No. 04-1350 (April 30, 2007).

The Office Action concedes that Tocci does not explicitly disclose a unit comprising apertures for sample loading or wells disposed below the apertures. (Office Action, page 6). The Office Action reasserts that it would have been obvious to one having ordinary skill in the art to modify the unit of Tocci by providing a row of apertures in the cover for sample loading, as taught by Elson *et al.*, because Elson *et al.* allegedly teaches the advantages of this design, in that it allegedly allows for a range of sample volumes and allows samples to be applied without opening the instrument. (Office Action, page 6). In addition, the Office Action asserts that in using the apertures taught by Elson *et al.* it would have been obvious to use the template carrier and templates

taught by Elson *et al.*, which are positioned in the gel matrix via the apertures, upon gelation (Office Action, pages 6-7).

In response to Applicants argument in the Response filed May 2, 2007, that there is no advantage or motivation for using the top wall of Elson in the device and method of Tocci, the Office Action asserts that the presence of sample loading ports in Elson allows accurate sample application without the need to disassemble the device for loading. The Applicants respectfully disagree with this assertion. There is a fundamental difference between Elson and Tocci, which clarifies why there is no advantage to using the top wall of Elson with the device of Tocci. The device of Tocci requires that a support medium is positioned on the tank without the lid in place, whereas in Elson, the gel is formed *in situ* with the top wall in place on the tank. Accordingly, there would be no reason to use a top wall with apertures in the device of Tocci because the top wall is not in place at the time samples are loaded using Tocci's device (i.e., just after the support medium is positioned on the tank). Therefore, using the top wall of Elson with the device of Tocci would lead to the nonsensical method of positioning a support on the tank and then securing a lid on the tank to enclose the support medium and then loading samples through apertures in the lid, rather than simply loading samples in wells of the support medium while the support medium was fully exposed after it was placed on the tank. Accordingly, there is no advantage of using a top wall with apertures with the device of Tocci.

In response to Applicants argument in the Response filed May 2, 2007 that there is no expectation of success in combining Elson with Tocci because Tocci provides no data to suggest that the device therein works appropriately, the Office Action asserts that there is no reason to believe that it would not function as disclosed. However, one reason to believe that it would not function as disclosed is that there is no consideration in Tocci of the fact that openings, and/or oxygen and hydrogen-absorbing material must be included in the buffer chambers to allow for the release of gas, which occurs from the electrodes during electrophoresis (See paragraph [0091] of the present specification for example). Thus, there is no consideration given in Tocci to the release of gas that occurs if the device is used for electrophoresis. Furthermore, there is no specific disclosure of Tocci to establish that a semi-solid electrophoresis buffer made according to the brief teaching therein, can be successfully employed to separate biomolecules with an electrophoresis gel. Finally, Tocci is not enabling for such a device and method, as no details are provided with respect to electrophoresis buffers that can be successfully employed in the semi-solid state.

In further support of the inventiveness of the present invention over the cited references, a number of secondary factors are present. For example, both of the cited references teach away from their combination. Tocci teaches that the top wall (i.e. lid) functions to close the tank to the atmosphere and to avoid evaporation (col. 3, lines 25-30; col. 4, lines 55-57; and col. 6, 12-17). The Office Action asserts in response to this argument that there is no reason to believe that a series of small apertures will destroy the ability of the lid to prevent substantial evaporation. However, Tocci teaches that a function of the lid is to close the tank from the atmosphere, which teaches directly against including apertures in the lid, especially when one considers that the top wall of Tocci is not attached to the tank when samples are typically loaded. Furthermore, Elson teaches away from devices that must be opened to the atmosphere before samples are loaded (Col. 1, lines 11-43), and the device of Tocci even with the lid of Elson is a device that needs to be opened to the atmosphere at the time of use to place the support medium on the tank. The Office Action in response to this argument asserts that teaching one way of performing a function is not a teaching away. However, Elson explicitly teaches away from using a device that must be opened to the atmosphere before samples are loaded (Col. 1, lines 11-43).

Another secondary factor that is provided by the current invention is the long-felt need of reduced time and expertise to perform electrophoresis experiments. More specifically, the present invention provides the long-felt need of an easy-to-use disposable cassette with an electrophoresis gel matrix, an anode and a cathode located therein, and apertures in a top wall above wells in the electrophoresis gel matrix, such that a customer can simply load samples through the apertures into the gel matrix without the need to assemble the gel system before use, for example by casting a gel, adding running buffers, and/or positioning a gel within the gel system and then closing the gel system. Using the present cassette and method, acceptable separation of biomolecules can be achieved with relatively few steps to conduct an electrophoresis experiment. Thus, an electrophoresis experiment can be performed in much less time and with less expertise, than previously required.

Another secondary factor present with respect to the pending claimed invention is commercial success. At least two companies have achieved commercial success in marketing products that fall under the pending claims. Invitrogen markets the E-Gel<sup>®</sup> (Exhibit A) products, which include all of the elements of pending independent claim 1. Lonza markets the FlashGel<sup>®</sup> system (Exhibit B), which include all of the elements of pending independent claim 1. As evidenced

by the attached product marketing information (Exhibits A and B), the commercial success of these products is based at least in part, on the reduced setup time and ease of use of the products due to the presence of the electrophoresis gel matrix, anode, and cathode within the cassette chamber, the disposable nature of the cassette, and the presence of apertures in the top wall of the cassette above wells in the gel matrix.

With respect to claims 2-4, 62, 85-87, 91 and 94-102, which depend from either independent claim 1 or 71, the combination of Tocci and Elson *et al.* does not render these dependent claims obvious either. Specifically, with respect to claims 2 and 94-98 the Applicants respectfully reassert, and the Office Action concedes, that Tocci discloses all regions are sealed before and during electrophoresis. Claims 2 and 94 presented herein recite that the third region in the disposable cassette is not sealed, while the first and/or second regions are sealed. The Office Action responds to this argument by indicating that the provision of loading apertures and wells in the electrophoresis region of Tocci leads to the 3<sup>rd</sup> region not being “sealed.” As indicated above, it is not obvious to use a lid with loading apertures above wells in the electrophoresis matrix of Tocci because there is no motivation to combine Tocci with Elson, no expectation of success in the combination, and several secondary factors including teaching away, long-felt need and commercial success. Thus, the combination of the cover of Elson *et al.* with the unit of Tocci does not render claims 2 and 94-98 obvious.

Regarding claims 87 and 91 presented herein, the separation medium of Tocci is positioned onto the central section, with the ends of the separation medium extending outward to lay on top of the reservoirs containing Tocci’s semi-solid buffer, thereby making electrical contact with the electrodes embedded in Tocci’s semi-solid buffer (see Figures 2-6). Thus, the Applicants respectfully reassert the electrodes of Tocci are not embedded in the electrophoresis matrix as asserted by the Office Action (Office Action, page 5).

Regarding claims 99 and 100 presented herein, the Applicants respectfully assert that the term “flat” refers to “having a surface that is without marked projections or depressions” (see Dictionary.com definition 3 at <http://dictionary.reference.com/browse/flat>). The bottom wall of Tocci has 2 large projections (See elements 6 and 7 of FIG. 3 of Tocci) on the bottom wall to accommodate the buffer vessels. The Office action asserts that the bottom wall of Tocci is flat because it includes several planar sections that are each flat. (Office Action, page 6). However, this assertion actually supports that the bottom wall of Tocci is not flat especially when considered in

view of FIG. 3 of Tocci considering the depth of elements 6 and 7. The claim language recites that the *bottom wall is flat*. Therefore, it is not enough that *regions within the bottom wall* of Tocci are flat.

In view of the above, the Applicants respectfully assert that the claims presented herein are not rendered obvious by the combination of Tocci and Elson *et al.*. Thus, the Applicants respectfully request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. §103(a) over Tocci in view of Elson *et al.*.

***Tocci (U.S. Patent No. 3,715,295) and Elson et al. (U.S. Patent No. 3,888,759) further in view of Pace (U.S. Patent No. 4,908,112)***

The Office Action, mailed July 27, 2007, rejected claims 5, 6, 63, 64, 75, and 88 under 35 U.S.C. §103(a) as allegedly being unpatentable over Tocci and Elson *et al.* in further view of Pace. The Applicants respectfully reassert that, as presented above, Tocci in combination with Elson *et al.* do not disclose a disposable cassette as recited in claims 1-4, 62, 71,85-87, 91 and 94-104 presented herein, and the Applicants respectfully assert that further combination with Pace does not render the Applicants disposable cassette obvious. Pace provides at most two embodiments of the capillary electrophoresis device, neither of which includes an electrophoresis gel matrix having one or more wells located below apertures in a top wall. Furthermore, Pace does not disclose a device having three regions, one region that includes the apertures and is located between a second region and a first region, wherein the second region and the first region include an electrode. Accordingly, the Applicant respectfully requests withdrawal of the rejection of claims 5, 6, 63, 64, 75, and 88 under 35 U.S.C. §103(a) as allegedly being unpatentable over Tocci and Elson *et al.* in further view of Pace.

***Tocci (U.S. Patent No. 3,715,295) and Elson et al. (U.S. Patent No. 3,888,759) in view of Eibl et al. (U.S. Patent No. 3,951,776)***

The Office Action, mailed July 27, 2007, reasserts the rejection of claims 7-9 under 35 U.S.C. §103(a) as allegedly being unpatentable over Tocci and Elson *et al.* in further view of Eibl. The Applicants respectfully reassert that, as presented above, Tocci in combination with Elson *et al.* do not disclose a disposable cassette as recited in claims 1-4, 62, 71,85-87, 91 and 94-104 presented herein, and the Applicants respectfully assert that further combination with Eibl *et al.* does not

render the Applicants disposable cassette obvious. Eibl *et al.* provide an electrophoresis apparatus that uses aluminum electrodes, but does not provide a disposable cassette having one or more apertures in a top wall. Furthermore, Eibl *et al.* do not disclose a device having three regions, one region that includes the apertures and is located between a second region and a first region, wherein the second region and the first region include an electrode. Accordingly, the Applicant respectfully requests withdrawal of the rejection of claims 7-9 under 35 U.S.C. §103(a) as allegedly being unpatentable over Tocci and Elson *et al.* in further view of Eibl *et al.*.

***Tocci (U.S. Patent No. 3,715,295) and Elson et al. (U.S. Patent No. 3,888,759) in view of Flesher et al. (U.S. Patent No. 4,773,984)***

The Office Action, mailed July 27, 2007, rejected claims 19-21 under 35 U.S.C. §103(a) as allegedly being unpatentable over Tocci and Elson *et al.* in further view of Flesher *et al.* The Applicants respectfully reassert that, as presented above, Tocci in combination with Elson *et al.* do not disclose a disposable cassette as recited in claims 1-4, 62, 71,85-87, 91 and 94-104 presented herein, and the Applicants respectfully assert that further combination with Flesher *et al.* does not render the Applicants disposable cassette obvious. Flesher *et al.* provide a vertical electrophoresis apparatus that can use palladium electrodes, but does not provide a disposable cassette having one or more apertures in a top wall. Also, Flesher *et al.* do not disclose a device having three regions, one region that includes the apertures and is located between a second region and a first region, wherein the second region and the first region include an electrode. Accordingly, the Applicant respectfully requests withdrawal of the rejection of claims 19-21 under 35 U.S.C. §103(a) as allegedly being unpatentable over Tocci. and Elson *et al.* in further view of Flesher *et al.*.

***Tocci (U.S. Patent No. 3,715,295) in view of Elson et al. (U.S. Patent No. 3,888,759) in further view of Day (UK Patent Application GB 2,284,484)***

The Office Action, mailed July 27, 2007, rejected claims 12-14 and 67-69 under 35 U.S.C. §103(a) as allegedly being unpatentable over Tocci and Elson *et al.* in further view of Day. The Applicants respectfully reassert that, as presented above, Tocci in combination with Elson *et al.* do not disclose a disposable cassette as recited in claims 1-4, 62, 71,85-87, 91 and 94-104 presented herein, and the Applicants respectfully assert that further combination with Day does not render the Applicants disposable cassette obvious because Day does not provide the missing elements of Tocci and Elson

et al.. Accordingly, the Applicant respectfully requests withdrawal of the rejection of claims 12-14 and 67-69 under 35 U.S.C. §103(a) as allegedly being unpatentable over Tocci. and Elson *et al.* in further view of Day.

***Tocci (U.S. Patent No. 3,715,295) in view of Elson et al. (U.S. Patent No. 3,888,759) in further view of Monthony et al. (U.S. Patent No. 3,948,743)***

The Office Action, mailed July 27, 2007, rejected claims 53, 56, 65, 79, 80, 81, 82, 89, 90 and 93 under 35 U.S.C. §103(a) as allegedly being unpatentable over Tocci and Elson *et al.* in further view of Monthony *et al.* The Applicants respectfully reassert that, as presented above, Tocci in combination with Elson *et al.* do not disclose a disposable cassette as recited in claims 1-4, 62, 71,85-87, 91 and 94-104 presented herein, and the Applicants respectfully assert that further combination with Monthony *et al.* does not render the Applicants disposable cassette obvious. Monthony *et al.* provide electrophoresis methods and buffers, but do not provide methods using a disposable cassette having one or more apertures in the top wall, or a gel matrix having one or more wells located below the apertures. Additionally, Monthony *et al.* do not disclose a device having three regions, one region that includes the apertures and is located between a second region and a first region, wherein the second region and the first region include an electrode. Accordingly, the Applicant respectfully requests withdrawal of the rejection of claims 53, 56, 65, 79, 80, 81, 82, 89, 90, 92 and 93 under 35 U.S.C. §103(a) as allegedly being unpatentable over Tocci and Elson *et al.* in further view of Monthony *et al.*.

***Tocci (U.S. Patent No. 3,715,295) in view of Elson et al. (U.S. Patent No. 3,888,759) and Monthony et al. (U.S. Patent No. 3,948,743) in further view of Pace (U.S. Patent No. 4,908,112)***

The Office Action, mailed July 27, 2007, rejected claims 54 and 55 under 35 U.S.C. §103(a) as allegedly being unpatentable over Tocci, Elson *et al.* and Monthony *et al.* in further view of Pace. The Applicants respectfully reassert that, as presented above, Tocci in combination with Elson *et al.* and Monthony *et al.* do not disclose a disposable cassette as recited in claims 53, 56, 65, 79, 80, 81, 82, 89, 90, 92 and 93 presented herein, and the Applicants respectfully assert that further combination with Monthony *et al.* does not render the Applicants disposable cassette obvious. Pace provides at most two embodiments of the capillary electrophoresis device, neither of which includes an electrophoresis gel matrix having one or more wells located below apertures in a top wall.



Furthermore, Pace does not disclose a device having three regions, one region that includes the apertures and is located between a second region and a first region, wherein the second region and the first region include an electrode. Accordingly, the Applicant respectfully requests withdrawal of the rejection of claims 54 and 55 under 35 U.S.C. §103(a) as allegedly being unpatentable over Tocci and Elson *et al.* and Monthony *et al.* in further view of Pace.

***Tocci (U.S. Patent No. 3,715,295) in view of Elson et al. (U.S. Patent No. 3,888,759) and Monthony et al. (U.S. Patent No. 3,948,743) in further view of Eibl et al. (U.S. Patent No. 3,951,776)***

The Office Action, mailed July 27, 2007, rejected claim 50 under 35 U.S.C. §103(a) as allegedly being unpatentable over Tocci, Elson *et al.* and Monthony *et al.* in further view of Eibl *et al.* The Applicants respectfully reassert that, as presented above, Tocci in combination with Elson *et al.* and Monthony *et al.* do not disclose a disposable cassette as recited in claims 53, 56, 65, 79, 80, 81, 82, 89, 90, 92 and 93 presented herein, and the Applicants respectfully assert that further combination with Eibl *et al.* does not render the Applicants disposable cassette obvious. Eibl *et al.* provide an electrophoresis apparatus that uses aluminum electrodes, but does not provide a disposable cassette having one or more apertures in a top wall. Furthermore, Eibl *et al.* do not disclose a device having three regions, one region that includes the apertures and is located between a second region and a first region, wherein the second region and the first region include an electrode. Accordingly, the Applicant respectfully requests withdrawal of the rejection of claim 50 under 35 U.S.C. §103(a) as allegedly being unpatentable over Tocci and Elson *et al.* and Monthony *et al.* in further view of Eibl *et al.*.

***Tocci (U.S. Patent No. 3,715,295) in view of Elson et al. (U.S. Patent No. 3,888,759) and Monthony et al. (U.S. Patent No. 3,948,743) in further view of Day et al. (UK Patent Application GB 2,284,484)***

The Office Action, mailed July 27, 2007, rejected claims 58-60 under 35 U.S.C. §103(a) as allegedly being unpatentable over Tocci, Elson *et al.* and Monthony *et al.* in further view of Day *et al.* The Applicants respectfully reassert that, as presented above, Tocci in combination with Elson *et al.* and Monthony *et al.* do not disclose a disposable cassette as recited in claims 53, 56, 65, 79, 80, 81, 82, 89, 90, 92 and 93 presented herein, and the Applicants respectfully assert that further

combination with Day does not provide the missing elements of this combination of references. Accordingly, the Applicant respectfully requests withdrawal of the rejection of claims 58-60 under 35 U.S.C. §103(a) as allegedly being unpatentable over Tocci and Elson *et al.* and Monthony *et al.* in further view of Day *et al.*.

#### ***VI. Allowable Subject Matter***

The Applicants respectfully acknowledge the Examiner's remarks regarding the allowable subject matter in allowing claim 77 and indicating that claims 18 and 73 would be allowable if rewritten in independent form.

#### **Conclusion**

In view of the foregoing amendments and remarks, the pending claims are deemed to be allowable, and their favorable reconsideration and allowance is respectfully requested. It is believed that this response requires the payment of \$790.00 for filing a Request for Continued Examination (RCE) and \$120.00 for one (1) month extension of time. A total of \$910.00 is due with this response. However, if additional fees or extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any additional or requisite fees are hereby authorized to be deducted from, or any overpayment credited to, Deposit Account No. 503994. Should the Examiner have any questions or comments as to the form, content or entry of this response, the Examiner is requested to contact the undersigned at the telephone number below.

Respectfully submitted,

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